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Bisphenol A and Child Vascular Health: A Preview of Future Heart Disease Risk?

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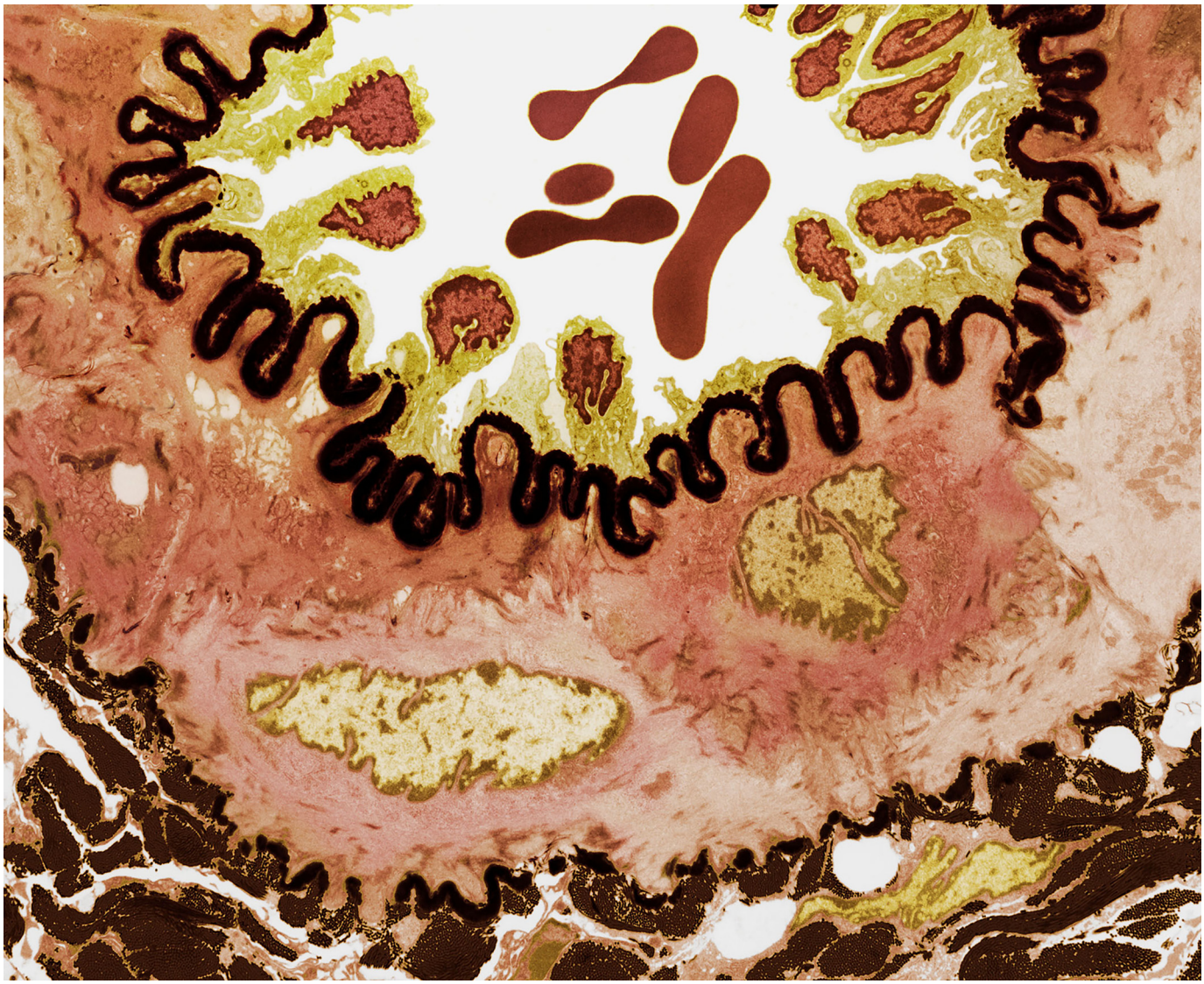
Exposures to phthalates and bisphenols have well-documented adverse effects on reproductive health and human development.[1] These endocrine-disrupting chemicals (EDCs) are also associated with obesity, hypertension, and blood vessel lesions in cross-sectional studies of adolescents and adults.[2–5] It is conceivable that processes leading to such damage start early in life and may be affected by prenatal chemical exposure.[6,7] A study recently published in *Environmental Health Perspectives* examined this question in children followed from gestation into childhood.[8]

The authors measured phthalates and bisphenols in urine samples from 935 pregnant Generation R participants during their first, second, and third trimesters. The Generation R Study, based in Rotterdam, the Netherlands, comprises a population-based prospective cohort.[9] At approximately 10 years of age, the women's children underwent ultrasounds for two measurements of the common carotid artery: distensibility (elasticity) and intima-media thickness (the thickness between the intima and media layers of the vessel wall). Both distensibility and intima-media thickness reflect vascular health in the whole body[10–12]; thicker vessel walls and reduced elasticity are considered distinct but overlapping risk factors for cardiovascular disease in adulthood, such as atherosclerosis.[13]

The authors analyzed the children's vascular measurements in association with their mothers' prenatal levels of three bisphenols [bisphenol A (BPA), bisphenol S (BPS), and bisphenol F (BPF)],



The intima layer of the artery (shown in black) is composed of endothelial cells, and the media layer (shown in pink) is made of smooth muscle and elastic fibers. Combined expansion (diastole) and contraction (systole) of the media layer pushes blood through the artery and controls blood pressure. In this transmission electron micrograph, the intima has accordioned due to contraction of the media. Image: © Steve Gschmeissner/Science Source.

low-molecular-weight phthalates as a group, high-molecular-weight phthalates, and three individual phthalates. They found no associations between any of the chemicals and distensibility. However, higher maternal urine concentrations of total bisphenols and of BPA alone were associated with thinner vessel walls in the children's carotid artery. No associations were found for BPS, BPF, or any phthalate.

The association of higher total bisphenol and BPA exposure with thinner—rather than thicker—vessel walls surprised the team initially but is biologically plausible, says first author Sophia Blaauwendraad. "Associations between higher BPA levels and atherosclerosis in adulthood [demonstrated in earlier studies[14]] could be due to oxidative stress that accelerates the formation of atherosclerotic plaques and thickens the vascular wall," says Blaauwendraad, a physician and graduate student in epidemiology under senior coauthor Vincent Jaddoe at Rotterdam's Erasmus University Medical Center. Fetal exposures, on the other hand, may be associated with an underdevelopment of the vasculature in childhood, the authors speculate. However, Blaauwendraad says, as yet no prospective studies have tracked intima-media thickness measures from childhood to adulthood.[15]

Nikki Posnack, an assistant professor of pharmacology, physiology, and pediatrics at Children's National Hospital in Washington, DC, says the study's strengths include its large sample size and measurements of several subtypes of phthalates and bisphenols at three different time points during pregnancy. Posnack, who was not involved in the research, says, "This is a compelling study that opens up new opportunities for mechanistic follow-up studies in model systems." Such studies could examine whether BPA disrupts development of blood vessels and alters their contractile properties,[16] similar to the chemical's disruption of hormonal regulation.

According to Lars Lind, a professor of medicine at Uppsala University in Sweden, who also was not involved in the project, studying the effect of the chemicals on early vascular changes in animal models would be worthwhile and should be accompanied by replication efforts in other human birth cohorts. "Since the findings were unexpected, replication is critical to increase our faith in them," says Lind. "But it is possible that these chemicals may have different effects at the fetal stage than later in life."

The association with total bisphenols appears to have been driven mainly by BPA; BPS and BPF were below the limit of detection in more than half the samples, possibly because they were collected in 2002–2006, when these chemicals were used less than today. However, human exposure to these BPA replacement chemicals has been increasing.[17] "With that in mind," Posnack says, "I think the study fills an important knowledge gap by exploring if exposure to any bisphenols *in utero* may affect subclinical indicators of vascular disease risk later in life."

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